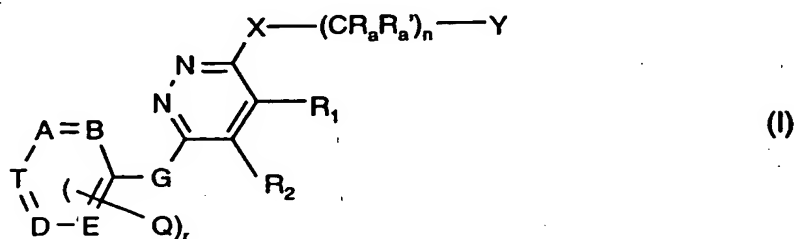


Abstract:

The invention relates to the treatment of an inflammatory disease, especially an inflammatory rheumatoid or rheumatic disease, and/or pain with an inhibitor of the activity of VEGF receptor tyrosine kinase of the formula I,



wherein

r is 0 to 2,

n is 0 to 3

R₁ and R₂

a) are independently in each case a lower alkyl;

b) together form a bridge of subformula I*,



wherein the bond is achieved via the two terminal C atoms and

m is 0 to 4, or

c) together form a bridge of subformula I**,



wherein one or two of the ring members T₁, T₂, T₃ and T₄ are nitrogen, and the others are in each case CH, and the bond is achieved via atoms T₁ and T₄;

G is -C(=O)-, -CHF-, -CF₂-, lower alkylene, C₂-C₆alkenylene, lower alkylene or C₃-C₆alkenylene substituted by acyloxy or hydroxy, -CH₂-O-, -CH₂-S-, -CH₂-NH-, -CH₂-O-CH₂-, -CH₂-S-CH₂-, -CH₂-NH-CH₂-, oxa (-O-), thia (-S-), imino (-NH-), -CH₂-O-CH₂-, -CH₂-S-CH₂- or

-CH₂-NH-CH₂-;

A, B, D, E and T are independently N or CH subject to the proviso that at least one and not more than three of these radicals are N;

Q is lower alkyl, lower alkoxy or halogen;

R_a and R_a' are each independently H or lower alkyl;

X is imino, oxa, or thia;

Y is hydrogen, aryl, heteroaryl, or unsubstituted or substituted cycloalkyl; and

Z is mono- or disubstituted amino, halogen, alkyl, substituted alkyl, hydroxy, etherified or esterified hydroxy, nitro, cyano, carboxy, esterified carboxy, alkanoyl, carbamoyl, N-mono- or N,N-disubstituted carbamoyl, amidino, guanidino, mercapto, sulfo, phenylthio, phenyl lower alkylthio, alkylphenylthio, phenylsulfinyl, phenyl-lower alkylsulfinyl, alkylphenylsulfinyl, phenylsulfonyl, phenyl-lower alkylsulfonyl, alkylphenylsulfonyl, or (alternatively or, in a broader aspect of the invention, in addition) selected from the group consisting of ureido, halo-lower alkylthio, halo-lower alkansulfonyl, pyrazolyl, lower-alkyl pyrazolyl and C₂-C₇alkenyl; wherein – if more than 1 radical Z ($m \geq 2$) is present – the substituents Z are selected independently from each other;

and wherein the bonds characterized in subformula I* by a wavy line are either single or double bonds;

or an N-oxide of said compound, wherein 1 or more N atoms carry an oxygen atom; or a pharmaceutically acceptable salt thereof;

as well as to new phthalazine derivatives; processes for the preparation thereof; the application thereof in a process for the treatment of the human or animal body; the use thereof for the treatment of a disease, especially a disease caused by ocular neovascularisation, such as age-related macula degeneration or diabetic retinopathy, or other diseases that respond to the inhibition of tyrosine kinases, such as a proliferative disease; a method for the treatment of such disease in mammals; and the use of such a compound for the manufacture of a pharmaceutical preparation for the treatment especially of a disease as mentioned above.